

**WHAT IS CLAIMED IS:**

1. A method for the introduction of an agent into cells of a tissue, said method comprising:
  - a) injecting the agent into tissue and
  - b) applying voltage pulses between needle electrodes disposed in the tissue so as to establish electric fields in cells of the tissue sufficient to cause electroporation of the cells, thereby introducing said agent into the cells, wherein the tissue is skin.
2. The method of claim 1, wherein the agent is injected either prior to, simultaneously with or after step b.
3. The method of claim 2, wherein the agent is injected locally into the tissue.
4. The method of claim 3, wherein the voltage pulses are applied to two of said electrodes disposed in the tissue.
5. The method of claim 1, wherein the voltage pulses are applied to at least two pairs of said electrodes simultaneously, sufficient to cause electroporation, thereby introducing said agent into said cells.
6. The method of claim 1, wherein said method is *in vivo*.
7. The method of claim 1, wherein the agent is selected from the group consisting of drugs, nucleic acids, polynucleotides, chemotherapeutic agents, peptides, polypeptides, and antibodies.
8. The method of claim 7, wherein the agent is a polynucleotide selected from the group consisting of DNA, cDNA and RNA sequences.

Sub C 2

Sub C 3

9. The method of claim 8, wherein the polynucleotide is an antisense nucleic acid or ribozyme.
10. The method of claim 8, wherein the polynucleotide encodes a protein selected from the group consisting of immunomodulatory agent, biological response modifier, metabolic enzyme, and antiangiogenesis compound.
11. The method of claim 10, wherein the polynucleotide encodes a biological response modifier that modifies the immune response.
12. The method of claim 8, wherein the polynucleotide is contained in a viral vector.
13. The method of claim 12, wherein the viral vector is selected from the group consisting of adenovirus, herpes virus, vaccinia, and retrovirus.
14. The method of claim 13, wherein the retroviral vector is a derivative of a murine or avian retrovirus.
15. The method of claim 7, wherein the agent is a chemotherapeutic agent.
16. The method of claim 15, wherein said chemotherapeutic agent is selected from the group consisting of bleomycin, neocarcinostatin, suramin, doxorubicin, carboplatin, taxol, mitomycin C and cisplatin.
17. The method of claim 1, wherein the cells are tumor cells.
18. The method of claim 17, wherein the cells are melanoma or basal cell carcinoma cells.

*Sub  
C4*

19. The method of claim 18, wherein the tumor cells are subsurface tumor cells.

*Sub  
CS*

20. The method of claim 1, wherein said tissue is mammalian.

21. The method of claim 20, wherein said tissue is human.

22. The method of claim 5, wherein said electrodes are contained in a four needle array of electrodes or a six needle array of electrodes.

23. The method of claim 1, wherein the electric field is from about 10 V/cm to 2000 V/cm.

*Sub  
C6*

24. The method of claim 1, wherein from about 1 to 100 electrical pulses are applied.

25. The method of claim 24 wherein the electrical pulses are from about 10  $\mu$ sec to 100 msec in duration.

26. The method of claim 1, wherein the electrical pulse is selected from the group consisting of a square wave pulse, an exponential wave pulse, a unipolar oscillating wave form of limited duration, and a bipolar oscillating wave form of limited duration.

27. The method of claim 26, wherein said electrical pulse is comprised of a square wave pulse.

28. A method for the introduction of an agent into cells of a tissue, said method comprising:

a) introducing the agent locally into tissue by a route other than dermal absorption, and

b) applying voltage pulses to electrodes disposed in the tissue so as to establish electric fields in the tissue sufficient to cause the agent to enter cells of the tissue, thereby introducing said agent into the cells,  
wherein the tissue is skin.

29. The method of claim 28, wherein the agent is injected either prior to, simultaneously with or after step b.

30. The method of claim 29, wherein the agent is introduced locally into tissue by local injection.

31. The method of claim 30, wherein the voltage pulses are applied to two of said electrodes disposed in the tissue.

32. The method of claim 30, wherein the voltage pulses are applied to at least two pairs of said electrodes simultaneously, sufficient to cause electroporation, thereby introducing said agent into said cells.

33. The method of claim 28, wherein said method is *in vivo*.

34. The method of claim 28, wherein the agent is selected from the group consisting of drugs, nucleic acids, polynucleotides, chemotherapeutic agents, peptides, polypeptides, and antibodies.

35. The method of claim 34, wherein the agent is a polynucleotide selected from the group consisting of DNA, cDNA and RNA sequences.

36. The method of claim 35, wherein the polynucleotide is an antisense nucleic acid or ribozyme.

37. The method of claim 35, wherein the polynucleotide encodes a protein selected from the group consisting of immunomodulatory agent, biological response modifier, metabolic enzyme, and antiangiogenesis compound.
38. The method of claim 37, wherein the polynucleotide encodes a biological response modifier that modifies the immune response.
39. The method of claim 35, wherein the polynucleotide is contained in a viral vector.
40. The method of claim 39, wherein the viral vector is selected from the group consisting of adenovirus, herpes virus, vaccinia, and retrovirus.
41. The method of claim 40, wherein the retroviral vector is a derivative of a murine or avian retrovirus.
42. The method of claim 34, wherein the agent is a chemotherapeutic agent.
43. The method of claim 42, wherein said chemotherapeutic agent is selected from the group consisting of bleomycin, neocarcinostatin, suramin, doxorubicin, carboplatin, taxol, mitomycin C and cisplatin.
44. The method of claim 28, wherein the cells are tumor cells.
45. The method of claim 44, wherein the cells are melanoma or basal cell carcinoma cells.
46. The method of claim 45, wherein the tumor cells are subsurface tumor cells.
47. The method of claim 28, wherein said tissue is mammalian.
48. The method of claim 47, wherein said tissue is human.

49. The method of claim 32, wherein said electrodes are contained in a four needle array of electrodes or a six needle array of electrodes.
50. The method of claim 28, wherein the electric field is from about 10 V/cm to 2000 V/cm.
51. The method of claim 28, wherein from about 1 to 100 electrical pulses are applied.
52. The method of claim 51 wherein the electrical pulses are from about 10  $\mu$ sec to 100 msec in duration.
53. The method of claim 28, wherein the electrical pulse is selected from the group consisting of a square wave pulse, an exponential wave pulse, a unipolar oscillating wave form of limited duration, and a bipolar oscillating wave form of limited duration.
54. The method of claim 53, wherein said electrical pulse is comprised of a square wave pulse.
55. The method of claim 28, wherein the route comprises rapid infusion.
56. The method of claim 28, wherein the route comprises nasopharyngeal absorption.
57. The method of claim 28, wherein the route comprises oral administration.

*add  
c1*